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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/561,292	08/08/2006	Lydie Bougueleret	DV/4-33628A	6538

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EXAMINER	
ARCHIE, NINA	

ART UNIT	PAPER NUMBER
1645	

MAIL DATE	DELIVERY MODE
12/22/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/561,292	BOUGUELERET ET AL.	
	Examiner	Art Unit	
	Nina A. Archie	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/6/2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-20* is/are pending in the application.

4a) Of the above claim(s) *8-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-7* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *8/8/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Priority

1. Applicant's claim for domestic priority under 35 U.S.C. 119(e) is acknowledged.

Drawings

2. The drawings in this application have been accepted. No further action by Applicant is required.

Specification

3. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Information Disclosure Statement

4. The information disclosure statement filed 8/8/2006 has been considered. An initialed copy is enclosed.

Election/Restrictions

Applicant's election with traverse of Group I claims 1-7 are acknowledged. The traversal is on the ground(s) of requesting a rejoinder of Groups 2-5, insofar as they apply to SEQ ID NO:3, since the screening and diagnosis methods of Group I directly implicate CPP (Cardiovascular disorder Plasma Polypeptides) polypeptides and anti-CPP antibodies. In the search for said screening and diagnosis methods in the art, the Examiner will inevitably be looking for CPP polypeptides and anti-CPP antibodies that can potentially be used to detect, e.g., SEQ ID NO: 3.

This is not found persuasive because the technical feature of Group 1 is anticipated by Tang et al WO/2002/70539-A2. Tang et al teach an isolated polypeptide comprising an amino acid sequence of SEQ ID NO: 4 (see claim 9 SEQ ID NO: 1250). Therefore lack unity of invention dated on 6/5/2008 is based on the claims filed. Furthermore, because the technical feature of Group I is anticipated by the art and

therefore not "special" within the meaning of PCT Rule 13.2. Applicant did not provide evidence as reason for not requesting election/restriction of Group I claims as they relate to the teachings of the reference.

The requirement is still deemed proper and is therefore made FINAL.

Claims 8-20 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions Group II (claims 8-9), Group III (claim 10), Group IV (claims 11-13), Group V (claim 14), Group VI (claim 15), Group VII (claim 16), Group VIII (claim 17), and Group IX (claims 18-20) there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the response filed 10-6-08.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1-7 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

The claims are drawn to a vast genus of fragments of a polypeptide and variants with at least 75% sequence identity. To fulfill the written description requirements set forth under 35 USC § 112, first paragraph, the specification must describe at least a substantial number of the members of the claimed genus, or alternatively describe a

representative member of the claimed genus, which shares a particularly defining feature common to at least a substantial number of the members of the claimed genus, which would enable the skilled artisan to immediately recognize and distinguish its members from others, so as to reasonably convey to the skilled artisan that Applicant has possession the claimed invention.

To adequately describe the genus of fragments of SEQ ID NO: 3 which is at least ten amino acids long; the genus of fragments of SEQ ID NO: 3 as a variant with at least 75% sequence identity having one or more amino acid substitutions, deletions or insertions relative to SEQ ID NO:3; the genus of variants with at least 75% of SEQ ID NO:3 as set forth supra applicant must also give a functional limitation of fragments of a polypeptide and variants with at least 75% sequence identity. Furthermore, open claim language of claim 1 which states “having one or more amino acid substitutions, deletions or insertions relative to SEQ ID NO:3” is interpreted as a replacement residue can be replaced with any amino acid residue.

The specification, however, does not disclose distinguishing and identifying features of a representative member of the genus of fragments of a polypeptide and variants with at least 75% sequence identity, to which the claims are drawn, such as a correlation between structure of the polypeptide and its recited function, so that the skilled artisan could immediately envision or recognize at least a substantial number of members of the claimed genus vast genus of fragments of a polypeptide and variants with at least 75% sequence identity..

Even though one could screen for which changes vast genus of fragments of a polypeptide and variants with at least 75% sequence identity, the courts have held that possession of a genus may not be shown by merely describing how to obtain members of the claimed genus or how to identify their common structural features. The written description requirement is separate and distinct from the enablement requirement (See also *Univ. of Rochester v. G.D. Searle & Co.*, 358 F.3d 916, 920-23, 69 USPQ2d 1886, 1890-93 (Fed. Cir. 2004) and adequate written description requires more than a mere reference to a potential method for identifying candidate polypeptides. In such an

unpredictable art, as set forth supra, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus. See *Noelle v Lederman*. 355 F. 3d 1343, 1350, 69 USPQ2d 1508, 1514 (*Fed. Cir. 2004*) and *In re Alonso* (Fed. Cir. 2008-1079).

The specification lacks written description of the genus of fragments of a polypeptide and variants with at least 75% sequence identity. For example, Colman et al. (Research in Immunology 145: 33-36, 1994, p.33 column 2, p. 35 column 1) disclose that a single amino acid changes in an antigen can effectively abolish the interaction with an antibody entirely and that a very conservative amino acid substitution may abolish antibody binding and a non-conservative amino substitution may have little effect in antibody binding. This underlies the importance of the description of the immunoepitopes that are protective and which conservative amino acid substitutions and where and how many changes can the immunoepitopes tolerate and still retain the ability to protect from infection.

MPEP § 2163.02 states, "an objective standard for determining compliance with the written description requirement is, 'does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed". The courts have decided: The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the "written description" inquiry, whatever is now claimed. See Vas-Cath, Inc.'v. Mahurkar, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (Federal Circuit, 1991). Furthermore, the written description provision of 35 USC § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993)and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

The Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "'Written Description" Requirement (66 FR 1099-1111, January 5,2001)

state, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (Id. at 1104).

The Guidelines further state, "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus" (Id. at 1106); accordingly, it follows that an adequate written description of a genus cannot be achieved in the absence of a disclosure of at least one species within the genus. Several publications document this unpredictability of the relationship between sequence and function, albeit that certain specific sequences may be found to be conserved over biomolecules of related function upon a significant amount of further research. Additionally Bowie et al (Science, 1990, 247:1306-1310) teach that an amino acid sequence encodes a message that determines the shape and function of a protein and that it is the ability of these proteins to fold into unique three-dimensional structures that allows them to function, carry out the instructions of the genome and form immunoepitopes. Bowie et al. further teach that the problem of predicting protein structure from sequence data and in turn utilizing predicted structural determinations to ascertain functional aspects of the protein is extremely complex. (column 1, page 1306). Bowie et al further teach that while it is known that many amino acid substitutions are possible in any given protein, the position within the protein's sequence where such amino acid substitutions can be made with a reasonable expectation of maintaining function are limited. Certain positions in the sequence are critical to the three dimensional structure/function relationship and these regions can tolerate only conservative substitutions or no substitutions (column 2, page 1306). Therefore, in accordance with the Guidelines, the description of fragments of a polypeptide and variants with at least 75% sequence identity is not deemed representative of the claimed invention thus the claim does not meet the written description requirement.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-7 rejected under 35 U.S.C. 102(a) as being anticipated by Murray et al WO 2002/079492A2 Date .

Claims 1-7 are drawn to a method of screening for and/or diagnosis of a cardiovascular disorder in a subject, comprising the steps of: a) detecting and/or quantifying the level of a polypeptide in a biological sample from said subject, wherein the polypeptide is selected from: i) a polypeptide comprising the amino acid sequence of SEQ ID NO:3; ii) a variant, with at least 75% sequence identity, having one or more amino acid substitutions, deletions or insertions relative to the amino acid sequence shown in SEQ ID NO: 3; and iii) a fragment of a polypeptide as defined in i) or ii) above which is a least ten amino acids long, and b) comparing said level to that of a control sample, wherein an increase in said level relative to that of the control is indicative of a cardiovascular disorder.

Murray et al teach a method of screening and or diagnosis, a method of predicting, or method of identifying a modulator, or a method for efficacy of treatment of cardiovascular disorder using polypeptide comprising SEQ ID NO: 3, polypeptide (SEQ ID NO: 32 see STIC results). Murray et al teach a method and its use for the prophylaxis and or treatment of cardiovascular disorders (angiogenesis-associated diseases) or for identifying a modulator. Murray et al teach a method of detecting an angiogenesis-associated transcript in a cell contacting a biological tissue sample with a polypeptide such as SEQ ID NO:3 (SEQ ID NO: 32 see STIC results). Murray et al teach samples comprising angiogenesis compared to control samples, wherein an increase in level relative

to that of the control is indicative of cardiovascular disorder or a risk of developing a cardiovascular disorder (see pgs. 2-4, 6, 15, 49, 37, 61-62, 81, 193 and 289-290 Example 2, abstract claims).

Murray et al teach method of screening and diagnosis for treatment angiogenesis-associated diseases which include heart disease and ischemia. Thus Murray et al inherently teach a method wherein cardiovascular disorder is Coronary Artery Disease. Murray et al teach a method wherein the biological sample such as blood or other bodily fluids thus inherently teaching plasma, wherein polypeptide is detected and or quantified by mass spectrometry, wherein polypeptide is detected and for quantified by Enzyme-Linked Immuno Sorbent Assay, wherein said detecting and/or quantifying the level of a polypeptide in a biological sample is performed ex vivo (see pgs. 2-4, 6, 15, 49, 37, 61-62, 81, 193 and 289-290 Example 2, abstract claims)..

Status of the Claims

No claims are allowed.

Claims 1-7 are rejected.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nina A. Archie whose telephone number is 571-272-9938. The examiner can normally be reached on Monday-Friday 8:30-5:00p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner supervisor, Robert Mondesi can be reached on 571-272-0956. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should

you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Nina Archie
Examiner
Art Unit 1645

/Robert B Mondesi/
Supervisory Patent Examiner, Art Unit 1645